

Amendments to the Drawings:

The attached drawing sheet 1/2 includes changes to Fig. 1. This sheet replaces the original sheet 1/2. In Fig. 1, sequence identifiers (SEQ ID numbers) have been added.

Attachments: Replacement Sheet
Annotated Sheet Showing Changes

REMARKS

Claims 1-16 and 19-25 are pending in the subject application. Of these, claims 19-23 have been withdrawn pursuant to a restriction requirement. Hereinabove, no claims have been canceled; claims 1, 7, 11, and 12 have been amended; and no new claims have been added. Therefore, claims 1-16 and 24-25, as amended, are now pending and under consideration. In view of the foregoing amendments and the following remarks, applicants respectfully request reconsideration of the objections and rejections set forth in the outstanding office action.

Applicants acknowledge the outstanding office action's indication that claim 10 is allowed.

The objection to the application on the grounds that the amino acid sequences on pages 5, 7, 11-13, 18-19, 21, 25, and 30-31 and in Figure 1 are not associated with a sequence identifier is respectfully traversed. Applicants have hereinabove amended the specification to add sequence identifiers. Applicants have also amended the drawings to add sequence identifiers to Figure 1. In view of these amendments to the specification and drawings, it is submitted that the objection to the application should be reconsidered and withdrawn.

The outstanding office action included a Notice to Comply With Requirements for Patent Applications Containing Nucleotide Sequences and/or Amino Acid Sequences. Applicants respectfully submit that The Notice to Comply does not specify

the defects with the Sequence Listing that was filed on October 10, 2006. In this regard, it is noted that Box 7 (entitled "Other") in the Notice to Comply was checked, but no explanation was given.

In response to the Notice to Comply, applicants submit herewith:

- (1) a substitute computer readable form of the "Sequence Listing";
- (2) a substitute paper copy of the "Sequence Listing"; and
- (3) a Statement in Accordance with 37 C.F.R. § 1.821(f) that the content of the paper and computer readable copies are the same and include no new matter.

Note that, in regard to item (2) above, applicants have hereinabove directed entry of the substitute paper copy of the "Sequence Listing" into the present application.

The objection to claims 1-9 and 24-25 because, in claim 1, the phrase "wherein said specific binding partner in not" should be "wherein said specific binding partner is not" is respectfully traversed. Applicants have amended claim 1 to correct this error. In view of the amendment to claim 1, it is submitted that the objection to claims 1-9 and 24-25 should be reconsidered and withdrawn.

The objection to claim 11 under 37 C.F.R. § 1.75 as being a substantial duplicate of claim 10 is respectfully traversed. Hereinabove, applicants have amended claim 11, and it is submitted that claim 11, as amended, is not a substantial duplicate of claim 10. Accordingly, the objection to claim 11 under 37 C.F.R. § 1.75 should be reconsidered and withdrawn.

The rejection of claims 1-9, 12-16, and 24-25 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement is respectfully traversed.

Applicants have amended claim 1 by incorporating the limitation of previous claim 7 into claim 1. In this regard, applicants' note that page 7, lines 19-23 of the application indicates that the term LSFAEPG includes sequences with no, one, two, three, four or five residues (other than the serine) conservatively substituted. For clarity, applicants have included this language explicitly in amended claim 1. Claim 1, as amended, specifies the nature of the phosphorylatable portion of the protein kinase substrate polypeptides, and applicants submit that this amendment, taken together with the following comments, addresses the concerns raised in the outstanding office action.

As set out on, for example, pages 2 and 3 of the application, the inventors have found a way of allowing the activity of many protein kinases to be screened using a common format. The inventors have surprisingly found that peptides that share a common epitope are phosphorylated efficiently by many different protein kinases, which fall into several different kinase subfamilies. This was unexpected, because

the prior art describes specific peptides as substrates for specific kinases, and a common epitope would not have been expected to have an appropriate conformation for phosphorylation by a range of protein kinases. This common epitope is specified in amended claim 1.

Further, not only can this common epitope be phosphorylated efficiently, but it is also the target for an effective phospho-specific antibody. Both the ability to be phosphorylated efficiently by many different protein kinases and the ability to be bound by an effective phospho-specific antibody contribute to the utility of the claimed polypeptides and kits. As set out on page 2, lines 10-22, of the application, there are no antibodies in existence that recognize phosphoserine or phosphothreonine (independent of the surrounding amino acid context) that are sufficiently good to be usable in assays of protein kinase activity: it has previously been necessary to develop separate phospho-specific antibodies for each serine/threonine phosphorylated substrate. The present invention overcomes this by provision of a phosphorylatable portion specified in amended claim 1 which is both an efficient substrate for many different protein kinases and a target for an effective phosphorylation-state sensitive antibody.

The consensus sequences of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:8, or SEQ ID NO:9 in claim 15 are adequately described. These consensus sequences are well known to those skilled in the art as being the sequences necessary for phosphorylation by the specified protein kinases. Demonstrating this, there are references cited on page 3 of

the specification that discuss three of these consensus sequences. The fourth sequence, Xaa-pSer-Xaa-Xaa-Ser, is also well known in the art and is discussed in, for example, Flotow et al., "Phosphate Groups as Substrate Determinants for Casein Kinase 1 Action," J. Biol. Chem. 265(24):14264-14269 (1990) (of record). There is no need for any narrower definition of the substrate sequences: one skilled in the art would have no difficulty whatsoever in understanding that applicants had possession of the invention, as the skilled artisan would fully understand that sequences defined in this way would have the desired properties.

For all the above reasons, it is submitted that there is ample written description of the claimed invention and that the rejection of claims 1-9, 12-16, and 24-25 under 35 U.S.C. § 112, first paragraph, should be reconsidered and withdrawn.

Applicants would like to comment on two issues raised in the outstanding office action in connection with its 35 U.S.C. § 112, first paragraph, rejection,

First, the PTO appears to have concluded erroneously that the claim required that the substrate polypeptides were not bound by antibodies directed to phosphotyrosine, phosphoserine or phosphothreonine. The above amendment to claim 1 is, in part, intended to clarify further that there is no requirement that the substrate polypeptides are not bound by antibodies directed to phosphotyrosine, phosphoserine or phosphothreonine. The requirement was intended to be that the two phosphorylatable portions were capable of being bound in a phosphorylation state-sensitive manner by a specific binding

partner that was not just an antibody specific for phosphotyrosine, phosphoserine or phosphothreonine.

Second, the PTO alleges that the specification fails to adequately describe the phosphorylation-state-sensitive binding partners. Applicants submit that the examples provide ample detailed experimental procedures for the generation of antibodies for use as binding partners. For example, the generation of anti LpSFAEPG antibodies are described in the application's Example 1. The inventors were clearly in possession of antibodies with the desired characteristics as shown in Figure 1, where the unphosphorylated forms of the peptides were unable to neutralize the antibodies generated by the described method, as discussed on page 32, line 13 to page 33, line 12 of the present application.

The rejection of claims 1-3, 6, and 8 under 35 U.S.C. § 102 (b) for anticipation by Albert et al., Molecular Biology of the Cell, 4th edition, pp. 176-178 (2002) ("Albert") is respectfully traversed.

Albert is an extract from a textbook describing protein phosphorylation in a cell. The PTO considers that any cell contains proteins that have binding partners that are sensitive to their phosphorylation state. A cell also contains many kinases, and, therefore, it contains two or more protein kinase substrates with different specificity conferring portions.

Applicants respectfully disagree with the PTO's characterization of Albert, with the PTO's construction of the claims, and with the PTO's conclusion as to anticipation.

Firstly, a cell clearly is not a kit and would not be considered by one skilled in the art to be a kit. There is nothing in the specification or the skilled artisan's understanding of the word "kit" that can in any way be taken to encompass a cell as discussed by Albert.

Secondly, the PTO has in no way indicated that the phosphorylatable portions of each polypeptide are capable of being bound in a phosphorylation state-sensitive manner by the same specific binding partner, a requirement that is in the claims but which the PTO totally fails to address. This is a key feature of the kit: as discussed above, this feature allows the same specific binding partner to be used to assess the phosphorylation state of the different kinase substrate polypeptides of the kit. Accordingly, Albert cannot deprive the previous claims, let alone amended claim 1, of novelty.

Thirdly, as noted above, applicants have amended claim 1 to include the limitations of previous claim 7. Previous claim 7 was not rejected for anticipation by Albert. Accordingly, claim 1 should likewise be novel over Albert.

For all of the above reasons, the rejection of claims 1-3, 6, and 8 under 35 U.S.C. § 102 (b) for anticipation by Albert should be reconsidered and withdrawn.

The rejection of claims 1-6, 8-9, and 24-25 under 35 U.S.C. § 102 (b) for anticipation by International Patent Application Publication No. WO 00/14536 of Tan et al. ("Tan") is respectfully traversed.

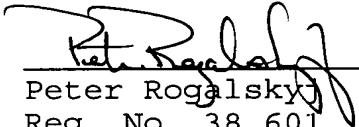
As noted above, applicants have amended claim 1 to include the limitations of previous claim 7. Previous claim 7 was not rejected for anticipation by Tan. Accordingly, claim

1 should likewise be novel over Tan. Claims 2-6, 8-9, and 24-25 depend from and further limit claim 1. Accordingly, claims 2-6, 8-9, and 24-25 should likewise be novel over Tan for at least the same reasons that claim 1 is novel over Tan. For at least these reasons, the rejection of claims 1-6, 8-9, and 24-25 under 35 U.S.C. § 102 (b) for anticipation by Tan should be reconsidered and withdrawn.

Withdrawn claims 19-23 are directed to methods which employ the kits and polypeptides of claims 1, 2, and 12. Since claims 1, 2, and 12 are patentable for all of the reasons set forth above, applicants submit that withdrawn claims 19-23 should now be rejoined and examined in the present application.

In view of the foregoing, it is submitted that this case is in condition for allowance, and such allowance is earnestly solicited.

Dated: October 23, 2007

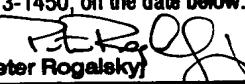

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10.23.07
Date


Peter Rogalsky

10 ng 100 ng

Competitor peptide



None

LpSFAEPG (SEQ ID NO:7)



RARTLSFAEPG (SEQ ID NO:16)



RARTLpSFAEPG (SEQ ID NO:26)

KKLNRTLSFAEPG (SEQ ID NO:13)



KKLNRTLS*FAEPG (SEQ ID NO:31)



RRRLSFAEPG (SEQ ID NO:4)



RRRLpSFAEPG (SEQ ID NO:27)

Sequence Identifiers
have been added.

Fig. 1